

REMARKS

Claims 1, 3, 5, 7-8, 11, 44, 46, 50, 54, 56, 58, 62, and 66 have been amended to further clarify the invention. Claim 4 has been canceled. The claim amendments and cancellations are made without prejudice to the filing of continuation applications. With these amendments, claims 1-3, 5-12 and 36-67 are pending. No new matter is added by the amendments.

Claims 1-12, and 36-67 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite; claim 3 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Reitz et al., *J. Med. Chem.* **1994**, 37(8), 1060-1062 ("Reitz"); claims 1, 2, 7-10, 36-45, 50-53, 56-57, and 62-65 stand rejected under 35 U.S.C. § 103 as being unpatentable over Prasad et al., *J. Med. Chem.* **1968**, 1144-1150 ("Prasad"); claims 1-10, 36-53, and 56-65 stand rejected under § 103 as being unpatentable over Morren et al., *Chemical Abstracts*, Vol. 59, No. 8732b ("Morren"); claims 1-2, 7-10, 36-45, 50-53, 56-57, and 62-65 stand rejected under § 103 over Mokrosz et al., *J. Med. Chem.* **1992**, 35, 2369-2374 ("Mokrosz"); claims 1-12, and 36-67 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent 5,859,246; claims 1, 3-6, 36-49, and 56-61 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent 6,172,229;

claims 1-10, 36-53, and 56-65 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent 6,426,347; and the specification is objected to as lacking the parent history.

Responsive to the obviousness-type double patenting rejections, Applicants enclose herewith a Terminal Disclaimer. Withdrawal of the rejections is therefore respectfully requested.

Applicants have amended the specification to indicate the priority claim. Withdrawal of the objection to the specification is therefore respectfully requested. The remaining rejections are addressed below.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully submit that the § 112, second paragraph rejections are overcome by the present claim amendments. These amendments are as follows.

Claims 1, 3, 7, 44, 46, 50, 56, 58, and 62 have been amended to specify the number of carbons in "alkyl," "alkylthio," "monoalkylamino," and "dialkylamino." Support for this amendment can be found on page 8 lines 22-25, and page 9, lines 1-2, and 5-6 of the specification as originally filed. Claim 4 has been cancelled and the subject matter of that claim has been added to claim 3 as a proviso.

Claim 5 has been amended to include "ethoxy" in the definition of R_2 , and "chloride" in the definition of R_3 . Consequently, claim 6 properly depends on claim 5. The phrase " R_2 and R_3 may not be 2-isopropoxyl and hydrogen, respectively, when R_1 is bromo;" has also been deleted from claim 5. Support for these amendments can be found in claims 3 and 4 as originally filed.

Claims 1, 3, 7, 9, 44, 46, 50, 54, 56, 58, 62, and 66 have been amended to specify assay conditions. Support for these amendment can be found on page 10, line 7 to page 11, line 2 of the specification.

Applicants respectfully submit that these amendments overcome all grounds of rejection based on 35 U.S.C. §112, second paragraph, and request withdrawal of the rejections.

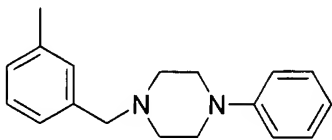
Rejection Under 35 U.S.C. § 102

Claim 3, as amended, overcomes the § 102(b) rejection based on Reitz.

Claim 4, which depended on Claim 3, has been canceled and the proviso from this canceled claim has been inserted into Claim 3. Consequently, the Reitz paper does not anticipate claim 3. Withdrawal of the rejection is therefore respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1, 2, 7-10, 36-45, 50-53, 56-57, and 62-65 stand rejected under § 103(a) as being obvious in view of Prasad. Specifically the Office has cited compound 101 of the Prasad reference, which has the formula:

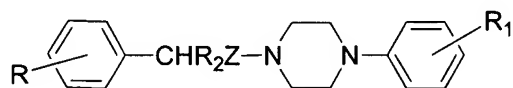


Applicants note initially that Prasad assigns no activity to this compound; thus, it cannot be determined whether the compound 101 is active or inactive. In this regard, Prasad does disclose inactive compounds. Further, the other listed compounds and their associated activity are insufficient to predict what activity compound 101 might display.

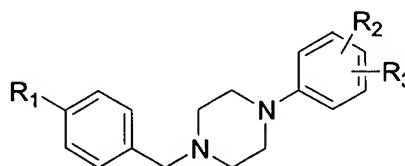
Claims 1, 7, 44, 50, 56, and 62 have been amended such that the R₂ and R₃ substituents are not simultaneously hydrogen. Support for the amendment may be found throughout the specification, including the example compounds on page 18, lines 1-13. Thus, claims 1, 7, 44, 50, 56, and 62 as amended (and the remaining pending claims which are dependent therefrom) are directed to compounds in which at least one of R₂ and R₃ is not hydrogen. In view of the lack of disclosed activity for Prasad's compound 101, the teachings of that reference do not provide a worker of ordinary skill in the art motivation to

synthesize the claimed compounds. Applicants respectfully request that the rejection based on Prasad under 35 U.S.C. 103(a) be withdrawn.

The Office has rejected claims 1-10, 36-53, and 56-65 under § 103(a) as being obvious in view of Morren. The Office alleges that the Morren reference discloses homologs of the compounds of the instant invention. Applicants note that Morren discloses compounds containing an optionally substituted C₃-C₅ carbon spacer (structure I below, Z is a C₂-C₄ group) whereas the claimed compounds require an unsubstituted methylene group (structure II below). Thus, Morren requires two carbons more between the piperazine and the phenyl than are permitted in the claimed compounds.



(I)



(II)

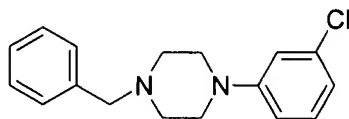
Moreover, the abstract of the Morren article points out that the maximum neurotropic activity was obtained with compounds that contain a butylene group substituted with a nitrile. The reference not only excludes the claimed compounds, but clearly expresses a preference for the butyl derivatives. While the compounds of the instant application may be somewhat

structurally related to the hypothetical class of compounds disclosed by the Morren reference they are certainly not homologs of the most active compounds. The preference of Morren for compounds that contain a butylene group substituted with a nitrile is without doubt a teaching away from a benzyl group on the piperazine.

One skilled in the art would use the most active compounds as a starting point or motivation to make other, hopefully more active, neurotropic agents. As a result, the compounds of the instant application would not have been obvious because they do not contain the minimum spacer required by Morren. At the time the instant invention was made, it would have been counter intuitive to use short spacers (methylene) to obtain neuroleptic activity when longer spacers had been demonstrated as being critical to generating improved activity than shorter spacers. Since Morren teaches away from the methylene spacer required by the claims, Morren certainly does not provide the requisite motivation to make the claimed compounds. Consequently, Applicants request that the 35 U.S.C. 103 (a) rejection based on the Morren reference be reconsidered and withdrawn.

Claims 1-2, 7-10, 36-45, 50-53, 56-57, and 62-65 stand rejected under § 103(a) as being unpatentable over Mokrosz. Mokrosz discloses as compound 23, cited by the Office, a

piperazine derivative that contains an unsubstituted benzyl at position 1.



Compound 23 of Mokrosz

The cited compound of Mokrosz differs from the claimed compounds by lacking a para substituent on the benzyl ring. Mokrosz does not suggest or imply any substituents on the benzyl group and therefore does not suggest the claimed compounds.

The applicants request that the 35 U.S.C. 103(a) based on Mokrosz be withdrawn.

Applicants respectfully submit that all requirements of Title 35 of the United States Code have been met. Allowance of the claims and passage of the case to issue are therefore respectfully solicited.

Should the Examiner believe a discussion of this matter would be helpful, the Examiner is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,

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